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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/964,178	09/25/2001	Robert Raffa	TUN-566US	9598

7590 07/01/2003

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EXAMINER
FONDA, KATHLEEN KAHLER

ART UNIT	PAPER NUMBER
1623	

DATE MAILED: 07/01/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/964,178	RAFFA ET AL.	
	Examiner	Art Unit	
	Kathleen Kahler Fonda, Ph.D.	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 May 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1-6,8-12, and 14-16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,8-12 and 1416* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-6, 8-12, and 14-16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

The claims as amended are indefinite because claim 1, from which all other pending claims depend, is internally inconsistent with regard to the exclusion of counterions having analgesic activity. Reading the claims in light of the specification (see the second full paragraph on page 7 of the specification), the oral dosage form of claim 1 is intended to include suspensions, elixirs, and solutions. When the glucosamine and the analgesic compound are together in a medium in which they can dissociate, the basic glucosamine and the acidic (in all recited species) analgesic compound will exist to a certain extent in ionized form, regardless of whether they

were introduced into the medium as two components of a single salt, or as two distinct salts each with different counterions. Thus, when the oral dosage form is a medium in which ions can dissociate, it is not seen how the claims can properly exclude "salts or complexes of glucosamine having a counterion which has an analgesic activity of its own," but still allow for analgesic compound to be a propionic acid analgesic such as ibuprofen or ketoprofen. The Examiner notes that a claim limited to a solid dosage form but otherwise the same would not suffer from this indefiniteness problem.

Claims 1-4 and 6 are again rejected, as set forth in the Office action of 02-13-03, under 35 U.S.C. 102(e) as being anticipated by GIORGETTI (B). Examples 14 and 31 of GIORGETTI show oral dosage forms comprising glucosamine salts of ketoprofen which meet the limitations of claim 6.

Applicant's arguments filed 05-05-03 have been fully considered but they are not persuasive. The argument that the reference does not apply because the claims have been amended to exclude "salts or complexes of glucosamine having a counterion which has an analgesic activity of its own" is not persuasive because, as explained above in the rejection under § 112, second paragraph, the claims are not clearly so limited.

Applicant's argument that the Examiner has improperly equated anti-inflammatory activity with analgesic activity is also not persuasive. The Examiner did not equate the two. Rather, the Examiner's conclusion that one would reasonably expect undiminished analgesic effect given the teaching of undiminished anti-inflammatory effect was based on the recognition that the ketoprofen anion remained intact. Thus the ketoprofen anion would be able to act in the known manner as an anti-inflammatory or an analgesic. Furthermore, the Examiner supports this conclusion with a quotation from column 4, lines 66-67: "Investigations in experimental animals evidenced a surprising increase in anti-inflammatory and analgesic activity."

Claims 1-5, 14, and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over PARADIES (AH).

Applicant claims an oral dosage form comprising glucosamine and ibuprofen, such that the analgesic efficiency of the dosage form is equal to or greater than that of the ibuprofen alone at the same dosage level.

Claim 2 of PARADIES recites a pharmaceutical composition comprising a salt of ibuprofen and an amino sugar which may be glucosamine. Reference claims 8-12 teach administration of

amounts within the scope of claim 15 to a subject suffering from pain, which is understood in context to mean a human subject. PARADIES also teaches that the composition may be in the form of an aqueous solution; see column 4, lines 5-8. PARADIES does not exemplify either an aqueous composition or a composition which comprises glucosamine.

It would have been obvious for a person of ordinary skill in the art at the time of the invention to choose glucosamine as the amino sugar, because PARADIES had taught that glucosamine was an amino sugar which could be so employed. It would furthermore have been obvious provide an aqueous composition, because PARADIES had taught that aqueous compositions could be used. If two ingredients known to be useful for pain relief (glucosamine and ibuprofen) are included in the composition, one ordinarily skilled in the art would expect the analgesic efficiency to be enhanced over ibuprofen alone, as required by pending claim 2. Applicant's attempt to limit the claims to exclude "salts or complexes of glucosamine having a counterion which has an analgesic activity of its own" does not distinguish over PARADIES for reasons set forth above in the rejection under § 112, second paragraph.

Claims 1-6, 8-12, and 14-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over PETRUS (A) in view of either GIORGETTI (B) or PARADIES (AH).

Applicant claims an oral dosage form comprising a glucosamine and an analgesic, which may be ibuprofen or ketoprofen, such that the analgesic efficiency of the dosage form is equal to or greater than that of the ibuprofen or ketoprofen alone at the same dosage level.

Example 1 of PETRUS teaches a dosage form comprising glucosamine sulfate and ibuprofen, wherein the weight ratio of glucosamine sulfate to ibuprofen is 4:1. Ibuprofen is an NSAID and a propionic acid analgesic. Example 5 of PETRUS teaches administration of the dosage form of Example 1 to a human patient suffering from rheumatoid arthritis, for relief of pain. Dosage amounts of instant claim 15 are taught by PETRUS at column 11, lines 34-38. Additional ingredients within the scope of those recited in instant claim 12 are also included in the dosage form of Example 1. PETRUS also teaches that ketoprofen is a known NSAID, useful for relieving inflammation, pain, and swelling; see column 4, lines 10-55. PETRUS does not teach an oral dosage form.

Each of GIORGETTI and PARADIES teaches as set forth above.

It would have been obvious for a person of ordinary skill in the art at the time of the invention to reformulate the composition of PETRUS as an oral dosage form. Motivation to do so is provided by each of GIORGETTI and PARADIES, which suggest oral dosage forms comprising glucosamine and an NSAID.

It would furthermore have been obvious to substitute ketoprofen for ibuprofen in the composition taught by PETRUS in Example 1. An ordinarily skilled artisan would have been motivated to do so with a reasonable expectation of success, because both ketoprofen and ibuprofen were known to be members of the same class of NSAID drugs, and both were known to be useful for pain management. Furthermore, since both are propionic acid analgesics, one of ordinary skill would reasonably have expected ketoprofen to be substitutable for ibuprofen in the dosage form such that the analgesic efficiency of the ketoprofen in the dosage form would not be diminished as compared to the that of the ketoprofen alone at the same dosage level. There would have been no expectation of any chemical reaction that might interfere with the efficacy of the ketoprofen.

Applicant's attempt to limit the claims to exclude "salts or complexes of glucosamine having a counterion which has an analgesic activity of its own" does not distinguish over

PARADIES for reasons set forth above in the rejection under § 112, second paragraph.

Claims 1, 2, 12, 14, and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over GIORGETTI (B).

Applicant claims a method to alleviate pain in a human subject by administering a dosage form comprising glucosamine and ketoprofen, such that the analgesic efficiency of the dosage form is equal to or greater than that of the ketoprofen alone at the same dosage level. Claim 12 recites an additional therapeutic amount of one or more of a number of different active agents.

GIORGETTI teaches as set forth above. GIORGETTI also teaches in claim 43 that the salts may be administered to mammals. GIORGETTI does not explicitly teach administration to a human. GIORGETTI also does not explicitly teach inclusion of additional active ingredients in an oral dosage form as required by claim 12.

It would have been obvious for a person of ordinary skill in the art at the time of the invention to administer the salt of GIORGETTI to a human. There would have been a reasonable expectation of success because a human is a mammal, and ketoprofen itself was well-known for human use. It would

furthermore have been obvious to include an additional active agent for the purpose of achieving the expect combination of benefits in a convenient form.

Applicant's arguments filed 05-05-03 have been fully considered but they are not persuasive. The arguments are the same as those regarding the anticipation rejection over GIORGETTI, and have been discussed above.

Papers relating to this application may be submitted to Technology Center 1600 by facsimile transmission. The number of the fax machine for official papers in Technology Center 1600 is (703) 308-4556. Any document submitted by facsimile transmission will be considered an official communication unless the cover sheet clearly indicates that it is an informal communication.

INTERNET INFORMATION: Secure and confidential access to patent application status information is now available; see http://www.uspto.gov/ebc/index.html for more information. Also, http://www.uspto.gov/web/offices/ac/comp/fin/clonedefault.htm may be used to pay patent maintenance fees, pay non-filing application fees, and maintain USPTO deposit accounts.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Kathleen

Kahler Fonda, at telephone number (703) 308-1620. Examiner Fonda can generally be reached Monday through Friday from 7:30 a.m. until 4:00 p.m. If the Examiner cannot be reached, questions may be addressed to Supervisory Patent Examiner James O. Wilson at (703) 308-4624. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-1235.

Kathleen Kahler Fonda, Ph.D., J.D.
Primary Examiner
Art Unit 1623